Claims

1. A method for identifying compounds useful in the treatment of diabetes, comprising determining a first amount of activity of a LKB1 polypeptide,
contacting the LKB1 polypeptide with a candidate pharmacological agent, and
determining the amount of activity of the contacted LKB1 polypeptide, wherein an increase in the amount of activity in the contacted LKB1 polypeptide relative to the first amount of activity of the LKB1 polypeptide is an indication that the candidate pharmacological agent is useful in the treatment of diabetes.

2. The method of claim 1, wherein the activity of the LKB1 polypeptide is measured by phosphorylation of AMP-activated kinase.

3. A method for identifying compounds useful in the treatment of diabetes, comprising
providing an assay mixture comprising a LKB1 polypeptide and a STRAD polypeptide that forms a heterodimer with the LKB1 polypeptide,
determining a first affinity of the dimeric interaction between LKB1 and STRAD,
contacting the assay mixture with a candidate pharmacological agent, and
determining a second affinity of the dimeric interaction between LKB1 and STRAD, wherein an increase in the second affinity relative to the second affinity is an indication that the candidate pharmacological agent is useful in the treatment of diabetes.

4. The method of claim 3, wherein the affinity of the dimeric interaction between LKB1 and STRAD is measured by co-immunoprecipitating LKB1 and STRAD, wherein an increase the amount of STRAD co-immunoprecipitating with LKB1 is indicative of an increase in the affinity of the dimeric interaction.

5. A method for identifying compounds useful in the treatment of cancer, comprising
determining a first amount of activity of an AMP-activated kinase polypeptide,
contacting the AMP-activated kinase polypeptide with a candidate pharmacological agent, and
determining the amount of activity of the contacted AMP-activated kinase polypeptide, wherein an increase in the amount of activity in the contacted AMP-activated

kinase polypeptide relative to the first amount of activity of the AMP-activated kinase polypeptide is an indication that the candidate pharmacological agent is useful in the treatment of cancer.

6. The method of claim 5, wherein the activity of the AMP-activated kinase polypeptide is measured by phosphorylation of acetyl CoA carboxylase.

7. A method for preparing a diabetes drug, comprising
identifying a compound that increases LKB activity and
formulating the compound for administration to a subject in need of such treatment.

8. The method of claim 7, wherein the diabetes is type II diabetes.

9. The method of claim 7, wherein the compound that increases LKB activity is identified by the method of claim 1.

10. A method for preparing a cancer drug, comprising
identifying a compound that increases AMP-activated kinase activity and
formulating the compound for administration to a subject in need of such treatment.

11. The method of claim 10, wherein the compound that increases LKB activity is identified by the method of claim 3.

12. A method for treating cancer, comprising
administering to a subject having a cancer characterized by reduced or absent LKB1 activity an effective amount of a compound that increases AMP-activated protein kinase (AMPK) activity in (cells of) the subject.

13. The method of claim 12, wherein the compound is an analog of adenosine monophosphate (AMP).

14. The method of claim 13, wherein the analog of AMP is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside (AICAR) or an analog or derivative thereof that increases AMPK activity.

15. The method of claim 14, wherein the analog or derivative of AICAR is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside monophosphate.

16. The method of claim 13, wherein the analog of AMP is adenosine.

17. The method of claim 12, wherein the compound is metformin or an analog or derivative thereof that increases AMPK activity.

18. The method of claim 12, wherein the compound is rosiglitazone or an analog or derivative thereof that increases AMPK activity.

19. The method of claim 12, wherein the compound is leptin or an analog or derivative thereof that increases AMPK activity.

20. The method of claim 12, wherein the compound is adiponectin or an analog or derivative thereof that increases AMPK activity.

21. The method of claim 12, wherein the reduction of LKB1 activity is due to the mutation or deletion of the LKB1 gene.

22. The method of claim 12, further comprising subjecting the cancer (cells) of the subject to a cell death stimulus.

23. A method for treating cancer, comprising

administering to a subject having a cancer characterized by reduced or absent LKB1 activity an effective amount of a compound that increases cellular AMP levels in (cells of) the subject.

24. The method of claim 23, wherein the compound is an analog of adenosine monophosphate (AMP).

25. The method of claim 24, wherein the analog of AMP is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside (AICAR) or an analog or derivative thereof that increases AMPK activity.

26. The method of claim 25, wherein the analog or derivative of AICAR is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside monophosphate.

27. The method of claim 24, wherein the analog of AMP is adenosine.

28. The method of claim 23, wherein the compound uncouples mitochondria.

29. The method of claim 23, wherein the reduction of LKB1 activity is due to the mutation or deletion of the LKB1 gene.

30. The method of claim 23, further comprising subjecting the cancer (cells) of the subject to a cell death stimulus.

31. A method for promoting apoptosis of cells having reduced or absent LKB1 activity, comprising

contacting the cells with a compound that is an activator of AMP-activated protein kinase (AMPK).

32. The method of claim 31, wherein the compound is an analog of AMP.

33. The method of claim 32, wherein the analog of AMP is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside (AICAR) or an analog or derivative thereof that increases AMPK activity.

34. The method of claim 33, wherein the analog or derivative of AICAR is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside monophosphate.

35. The method of claim 32, wherein the analog of AMP is adenosine.

36. The method of claim 31, wherein the compound is metformin or an analog or derivative thereof that increases AMPK activity.

37. The method of claim 31, wherein the compound is rosiglitazone or an analog or derivative thereof that increases AMPK activity.

38. The method of claim 31, wherein the compound is leptin or an analog or derivative thereof that increases AMPK activity.

39. The method of claim 31, wherein the compound is adiponectin or an analog or derivative thereof that increases AMPK activity.

40. The method of claim 31, wherein the reduction of LKB1 activity is due to the mutation or deletion of the LKB1 gene.

41. A method for promoting apoptosis of cells having reduced or absent LKB1 activity, comprising

contacting the cells with a compound that increases cellular AMP levels.

42. The method of claim 41, wherein the compound is an analog of adenosine monophosphate (AMP).

43. The method of claim 42, wherein the analog of AMP is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside (AICAR) or an analog or derivative thereof that increases AMPK activity.

44. The method of claim 43, wherein the analog or derivative of AICAR is 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside monophosphate.

45. The method of claim 42, wherein the analog of AMP is adenosine.

46. The method of claim 41, wherein the compound uncouples mitochondria.

47. The method of claim 41, wherein the reduction of LKB1 activity is due to the mutation or deletion of the LKB1 gene.

48. A method for treating a subject having or suspected of having diabetes comprising:

administering to a subject in need of such treatment an effective amount of an agent that increases the activity of LKB1 in the subject, as a treatment for the diabetes.

49. The method of claim 48, wherein the diabetes is type I diabetes.

50. The method of claim 48, wherein the diabetes is type II diabetes.

51. The method of claim 48, wherein the agent increases the kinase activity of LKB1.

52. The method of claim 48, wherein the agent increases the amount of LKB1.

53. The method of claim 48, wherein the agent increases the amount of STRAD.

54. The method of claim 48, wherein the agent increases the affinity of the dimeric interaction between LKB1 and STRAD.

55. A method for treating cancer, comprising

administering to a subject having a cancer characterized by reduced or absent LKB1 activity an effective amount of a compound that increases mTOR activity in (cells of) the subject.

56. The method of claim 55, wherein the agent decreases the kinase activity of mTOR polypeptide.

57. The method of claim 56, wherein the agent that decreases the kinase activity of mTOR polypeptide is rapamycin (sirolimus), a rapamycin analog or derivative, a salt thereof, or a solvate thereof.

58. The method of claim 57, wherein the rapamycin analog or derivative is everolimus (RAD-001), or rapamycin 42-ester with 3-hydroxy-2- (hydroxymethyl)-2- methylpropionic acid (CCI-779).

59. The method of claim 55, wherein the agent decreases the amount of mTOR polypeptide.

60. The method of claim 59, wherein the agent that decreases the amount of mTOR polypeptide is a siRNA/RNAi molecule or an antisense nucleic acid molecule.

61. The method of claim 55, further comprising subjecting the cancer (cells) of the subject to a cell death stimulus.

62. The method of claim 55, wherein the reduction of LKB1 activity is due to the mutation or deletion of the LKB1 gene.

63. A method for promoting apoptosis of cells having reduced or absent LKB1 activity, comprising

contacting the cells with an amount of a compound that is an activator of AMP-activated protein kinase (AMPK) effective to promote apoptosis.

64. The method of claim 63, wherein the agent decreases the kinase activity of mTOR polypeptide.

65. The method of claim 64, wherein the agent that decreases the kinase activity of mTOR polypeptide is rapamycin (sirolimus), a rapamycin analog or derivative, a salt thereof, or a solvate thereof.

66. The method of claim 65, wherein the rapamycin analog or derivative is everolimus (RAD-001), or rapamycin 42-ester with 3-hydroxy-2- (hydroxymethyl)-2- methylpropionic acid (CCI-779).

67. The method of claim 63, wherein the agent decreases the amount of mTOR polypeptide.

68. The method of claim 67, wherein the agent that decreases the amount of mTOR polypeptide is a siRNA/RNAi molecule or an antisense nucleic acid molecule.

69. The method of claim 63, further comprising subjecting the cancer (cells) of the subject to a cell death stimulus.

70. The method of claim 63, wherein the reduction of LKB1 activity is due to the mutation or deletion of the LKB1 gene.